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SANTA BARBARA • SANTA CRUZ

DEPARTMENT OF BIOLOGICAL CHEMISTRY  
SCHOOL OF MEDICINE  
THE CENTER FOR THE HEALTH SCIENCES

March 26, 1964

Dr. Joshua Lederberg  
Department of Genetics  
School of Medicine  
Stanford University  
Palo Alto, California

Dear Josh:

Thanks very much indeed for your kind words and your very thoughtful letter with results of the studies you have been able to make thus far on sequence comparisons in proteins.

I believe that such comparisons will become exceedingly fruitful when we have more information. The obvious trouble at the moment is that we know the sequences of so few proteins that it is extremely difficult to make generalizations. From time to time I have played with these comparisons and have abandoned them, simply because the few proteins whose sequence we know are not a very representative sample. This is, of course, why we have concentrated so much effort on the cytochromes. Indeed, since I talked in San Francisco, a number of rather novel and startling features of the cytochrome structure have been apparent. I am still struggling to milk as much as we can out of the replacement and non-replacement information. Again, we still have no clear notion as to the exact function of certain amino acid side chains, so that in parallel with considering protein sequence, I have been concerned with this other problem as well. I am presently playing with a couple of tentative drafts of the notions which have occurred to me. When I have these done I shall send them along. It would be helpful to have your views on the problems that emerge from our present ignorance and first guesses.

With all very best regards,

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Emil".

Emil L. Smith  
Chairman

ELS:B

EMIL  
SMITH